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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/202,805	05/07/99	WAGNER R	4-20921/APCT

001095
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EXAMINER	
DI NOLA BARON,I	
ART UNIT	**PAPER NUMBER**
1615	10

DATE MAILED: 09/18/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/202,805	Applicant(s) WAGNER ET AL.	
	Examiner Liliana Di Nola-Baron	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☒ Responsive to communication(s) filed on *31 July 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25 and 28-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25 and 28-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☒ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☒ received.

2.☐ received in Application No. (Series Code / Serial Number) _____.

3.☒ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

1. The examiner acknowledges the receipt of the Amendment filed on July 31, 2000. Applicant's arguments with respect to claims 1-25 and 28 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-25 and 28-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fujimura et al. in view of Ku et al. The claimed inventions relate to a compressed solid dosage form, comprising as active agent valsartan or a pharmaceutically acceptable salt thereof, or a combination of valsartan or a pharmaceutically acceptable salt thereof and hydrochlorothiazide, and at least one additive, a process of forming said dosage form, coprimates and granulates obtained according to said process and a method of treatment comprising administering said dosage form.

Fujimura et al. describes a method of treating hypertensive rats with a single p.o. administration of valsartan only and in combination with thiazide and nifedipine. Fujimura et al. teaches that systolic blood pressure of Spontaneously Hypertensive Rats is depressed by the single p.o. administration of valsartan only at a dosage of 3 mg./kg and in combination with thiazide

(5mg/kg) and nifedipine (1mg/kg) and concludes that potentiation of the effect of valsartan is significant in the combination with thiazide (See e.g., abstract). Fujimura et al. does not provide the process for the preparation of the dosage forms of valsartan.

Ku et al. discloses pharmaceutical compositions of irbesartan, containing as active ingredients irbesartan alone or in combination with a diuretic such as hydrochlorothiazide (See e.g., col.1, lines 38-41) Ku et al. characterizes irbesartan as a potent, long-acting angiotensin II receptor antagonist, which is particularly useful in the treatment of cardiovascular ailments such as hypertension and heart failure (See e.g., col.1, lines 19-23). Ku et al. provides pharmaceutical compositions, especially suitable for forming tablets, comprising 20-70% by weight irbesartan and optionally 2-33% diuretic and teaches that the compositions of the invention can be compressed on high speed tableting equipment to form small tablets (See e.g., col. 2, lines 5-56). Ku et al. teaches that the diuretic may be hydrochlorothiazide and describes pharmaceutical compositions of irbesartan, especially suitable for forming tablets, in which microcrystalline cellulose may be employed as diluent or disintegrant in the range of 5-15% and PVP may be used as binder (See e.g., col. 3, line 25 to col.4, lines 20). Ku et al. teaches that tablets may be prepared from the compositions of the invention by any suitable method, and brings as an example a process, which comprises preparing an intragranular composition by mixing the irbesartan, diuretic (for combined tablets) and additives to form a blend, optionally sizing the blend, re-mixing, granulating using a high shear mixer/granulator, drying the granules in a fluid bed dryer, sizing the granules by milling or screening, preparing a mixture of the sized granules with an extragranular composition and compressing the mixture to form tablets (See e.g., col. 6, lines 26-64). Ku et al. teaches that sizing the blend to break up aggregates after mixing the

irbesartan, diuretic and additives is optional (See e.g., col. 6, lines 33-42). Ku et al. teaches that the tablets of the invention contain 25 to 300mg of irbesartan and, for combined tablets, preferably 6.25 to 25 mg of hydrochlorothiazide, and the compositions of the invention may be used to prepare beads and granules (See e.g., col.7, lines 5-16). In Example 1 Ku et al. teaches that the size of the dried granules is 1 to 3 mm. Ku et al. teaches that the pharmaceutical compositions containing irbesartan may be used to treat or prevent disorders, including cardiovascular disorders, venous insufficiency, glaucoma, diabetic retinopathy, renal insufficiency and various complains of the central nervous system (See e.g., col.7, lines 17-23). Ku et al. teaches that an antiadherent is added to the composition in order to reduce the stickiness of irbesartan (See e.g., col. 4, lines 21-30). The examiner notes that such an addition is necessary because of the physical properties of the compound, but is not crucial for the purpose of preparing the tablets of the invention.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to synthesize a compressed solid dosage form of valsartan or valsartan and hydrochlorothiazide, as disclosed by Fujimura et al., using the method described by Ku et al. One having ordinary skill in the art would have been motivated to synthesize such dosage forms to produce small, easily swallowed and highly efficient tablets of valsartan or valsartan and hydrochlorothiazide in large scale, achieve a faster disintegration rate of the oral preparation and optimize the dosage of valsartan for an effective treatment of hypertensive disorders. Because of the teachings of Ku et al., that irbesartan is a potent angiotensin II receptor antagonist, and the teachings of Fujimura et al., that valsartan is an angiotensin II receptor antagonist, one having ordinary skill in the art would have a reasonable expectation that the method described by Ku et

al. for pharmaceutical compositions containing irbesartan would be successfully applicable to pharmaceutical compositions containing valsartan. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Liliana Di Nola-Baron whose telephone number is 703-308-8318. The examiner can normally be reached on Monday through Friday, 6:30AM-3:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3592 for regular communications and 703-305-3592 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 308-1234/ 1235.

September 14, 2000

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600